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ORIGINAL ARTICLES

THE OCCURRENCE OF ANKLE-CLONUS WITHOUT GROSS DISEASE OF THE CENTRAL NERVOUS SYSTEM.

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For a long time ankle-clonus passed as one of the most certain signs of organic disease of the central nervous system, and some authors even asserted that it did not occur in the absence of such disease. In 1879, however, Strümpell[1] pointed out that clonus occurs with considerable frequency in consumptives, in severe cases of typhoid, and in emaciated, weak patients, without other signs pointing to disease of the nervous system, excepting hyperesthesia of the skin and muscles.

It is the purpose of the present article to point out what conditions may be accompanied by ankle-clonus without other evidence suggestive of disease of the nervous system, to present a few illustrative cases, including one in which an autopsy revealed slight microscopic changes in the medulla oblongata, and to discuss the importance of clonus in diagnosis and prognosis. This is desirable for the reason that the subject is not fully treated in the text-books of medicine and neurology.

The Theory of Ankle-clonus. By ankle-clonus in this article is understood the true ankle-clonus, in which, on continuous upward pressure being made on the sole of the foot, there is a series of rhythmical oscillations in plantar flexion and extension, occurring with a frequency of from five to seven in the second, and continuing for a considerable period, often in fact so long as the pressure is maintained. Cases of so-called false clonus, in which a few irregular

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[1] Zur Kenntniss d. Sehnenreflexe, Deutsch. Arch. f. klin. Med., 1879, xxiv, 188.

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contractions take place, are not included. True ankle-clonus is never found in normal persons, and when present is usually associated with exaggeration of the tendon reflexes. It is rarely present in cases showing increased tendon reflexes due to functional conditions (neurasthenia, etc.), but is frequently observed in organic disease of the cord or brain, on which account it has been assigned considerable diagnostic importance. Clonus is also found, but less frequently, in other situations, especially the knee and jaw. In animals a closely analogous phenomenon is encountered in the so-called scratch reflex, so thoroughly studied by Sherrington.[2] Here in response to a continuous electric stimulation of the skin a series of rhythmical movements of the leg takes place, having a frequency of four in a second. Absolute regularity of the contractions is present in both conditions, and has been shown in the case of the scratch reflex to be due to the presence of a refractory phase, during which stimulation fails to elicit a muscular contraction. The path of the reflex may be assumed to be from the sensory fibers in the gastrocnemius muscle to the lumbar cord, and thence back again to the muscle by its motor nerve. But the reflex is of course more complicated than this, involving coincident inhibition of the antagonistic muscles, and a later contraction of these muscles to bring the foot back to the original position. The close analogy with the scratch reflex, which has been shown to be a spinal reflex, makes it probable that the cerebral cortex is not directly concerned in the production of clonus.

Ankle-clonus in Infectious Diseases Without Gross Lesions of the Central Nervous System. In pulmonary tuberculosis, Strümpell, as already stated, was the first to note the presence of ankle-clonus. He found it of fairly frequent occurrence, especially in emaciated subjects. Longard[3] seems to be the only writer to have made an extensive study of the subject, finding it present in 30 of 82 tuberculous cases, but in only 7 of these was clonus associated with a general increase of the tendon reflexes. Six of these 7 were emaciated and febrile, the other was neither. In 8 cases clonus was noticed in well-nourished patients. He makes no mention of the stage of lung involvement, but from the fact that his cases were observed in a general hospital it may be assumed that they were in an advanced stage. Personally I have not met with clonus in incipient tuberculosis, but only in cases in the last stage.

In typhoid fever the reflexes have been more thoroughly investigated, especially by the French. Remlinger[4] found ankle-clonus in 21 out of 100 cases, but in some of these the clonus was only "suggested." In these 21 cases with clonus the tendon reflexes were increased in 16, normal in 2, diminished in 2, and absent in 1.

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[2] The Integrative Action of the Nervous System, London, 1906.

[3] Deutsch. Zeitschr. f. Nervenheilk., 1891, i, 300.

[4] Rev. de Méd., 1901, xxi, 46.

The plantar reflexes were normal in all. The period of the disease in which clonus was first noted was variable, the phenomenon occurring with about equal frequency in the early stage, at the height of the fever, and during defervescence. It is important to note that clonus was more frequent in the severe cases, indicating a high grade of toxemia, for the mortality in the cases with clonus was 28.6 per cent., almost three times that of the cases without clonus (10 per cent.).

In other infectious diseases, such as septicemia (Case I of this paper), pneumonia, dysentery, cholera, malignant syphilis, the occasional presence of clonus has been noted, but no systematic studies have been made.

The following cases observed by the writer will serve to illustrate the occurrence of clonus in infectious diseases. The first is of particular interest because it is one of the few in which a postmortem examination of the central nervous system has been made.

CASE I.—*Septicemia following sinus thrombosis; marked clonus of ankle and jaw; autopsy; no meningitis nor gross lesions of central nervous system; moderate degenerative changes in pons and small foci of myelitis not involving pyramidal tracts.*

F. E., a female, aged fourteen years, entered the Massachusetts Charitable Eye and Ear Infirmary March 28, 1909, suffering from mastoiditis and sinus thrombosis, for which an operation was performed. There followed an intermittent fever, which continued until the death of the patient, April 15. When seen by the writer, April 12, there was marked emaciation, the head was retracted and stiff, and Kernig's sign was present. There was a marked and continuous clonus of the jaw and of both ankles, and the knee-jerks were increased. The plantar reflexes were normal, and there was no spasticity of the legs. Lumbar puncture on two occasions yielded a clear fluid of normal pressure and sterile on cultures. On the fourteenth day the patient had fallen into a condition of stupor. The jaw clonus was less marked, and the ankle-clonus was present on the right side, but only suggested on the left. She died April 15. At the autopsy (Dr. Verhoeff) there was found suppurative mastoiditis, with thrombosis of the lateral sinus at the site of operation, and intense venous congestion and edema of the cerebral pia-arachnoid, but no signs of meningitis; the spinal cord was not examined. There were septic endocarditis of the mitral valve and septic infarcts in the lungs, spleen, and kidneys. There was pus in both pleural cavities. From the spleen the streptococcus was obtained in pure culture.

Microscopic Examination: Unfortunately only the medulla oblongata was available for microscopic study. For the notes the writer is indebted to Prof. E. E. Southard, of the Harvard Medical School: "The positive findings were two in number: (1) A generalized diffuse blackening of the fibers in the white matter wherever examined, of a sort to suggest curable toxic changes rather than incurably destructive degeneration, and (2) foci of exudative myelitis, in general of an exceedingly mild character, but in one instance striking and associated with alterations in the nerve tissue itself.

"To begin with the focal lesion, we find the meshes of the sheath of the posterior median artery in the posterior median septum densely filled with mononuclear cells, including a few pigment-bearing cells, a small but somewhat larger number of endothelial cells containing mononuclear cells, great numbers of lymphocytes, and a number of plasma cells. The endothelium of the posterior median artery had been largely stripped away and lost. One other small artery in the lateral segment of the bulb was found invested with a slender amount of exudate. The others, including the meningeal arteries were quite free from exudate.

"There is no evidence of spread of exudate into the neighboring bulb tissue. The nerve cells of both nuclei of Goll do not stain properly, but neither do any other nerve cells seen elsewhere look as nerve cells should."

CASE II.—*Severe typhoid fever in a girl, aged eight years; massive hemorrhages on twenty-fifth day, followed by marked ankle-clonus; direct transfusion of blood, with prompt improvement, and disappearance of ankle-clonus in five days.*

B. C., a female child, aged eight years, entered the New Haven Hospital September 7, 1910 (service of Dr. C. J. Bartlett), with typhoid fever. At entrance the knee-jerks were normal. The disease ran a severe course, and on September 25, the twenty-fifth day of the disease, there were two profuse hemorrhages from the bowels. When seen by the writer the next day the child appeared exsanguinated, restless, dyspneic, and thirsty, but was conscious. There was marked and continuous ankle-clonus on both sides, the Achilles and patellar reflexes were greatly increased, but the Babinski and Oppenheim phenomena were both negative and the abdominal reflexes were normal. There was no spasticity. There were no signs of meningitis nor of other disease of the central nervous system. The same day the operation of direct transfusion of blood was performed, with immediate improvement in the alarming condition. The clonus persisted until October 1, when it disappeared and remained absent thereafter. Recovery was uneventful and complete.

CASE III.—*Girl, aged fifteen years; in last stages of phthisis; ankle-clonus five days before death.*

E. K., Russian Jewess, entered the Channing Home for Consumptives October 4, 1903, and died October 9, 1903. Duration of symptoms four months. Physical examination showed an emaciated girl, too weak to sit up. There were signs of extensive consolidation and a cavity on the right side, and of less extensive involvement of the left lung. There was a typical ankle-clonus on the right side and a slight one on the left. The knee-jerks were increased; the sensation was normal.

CASE IV.—*Girl, aged seventeen years; in third stage of phthisis; ankle-clonus six weeks before death.*

A. E. F., an Irish girl, entered the Channing Home for Consumptives August 31, 1903, with symptoms of three months' duration, and died November 29, 1903. She had lost fourteen pounds in weight, but was still fairly nourished. Temperature, 102°, pulse, 140. The process advanced rapidly, and in a month after admission there was complete consolidation of the right lung and of the left upper lobe. Tubercle bacilli were found in the sputum. Ankle-clonus was found on both sides, with marked exaggeration of the knee-jerks. Four days later the clonus was well marked on the right side, but only slight on the left.

Cases like the foregoing are not uncommon, but heretofore have not been generally recognized. It will be noticed that the clonus may be either one-sided or bilateral, and does not usually persist for more than a few days or weeks. In the writer's experience clonus has been more frequent in the young and in the female sex, but this may be due to the nature of the clinical material.

Ankle-clonus in Cachexia. Sternberg[5] mentions clonus in weak, emaciated patients afflicted with malignant disease and "senile marasmus."

Ankle-clonus in Various Intoxications. In uremia ankle-clonus is not uncommon, and, as Curschmann[6] pointed out, may in chronic cases, come on several days before the uremic seizure, thus furnishing a valuable prognostic indication. Lion[7] also found a marked increase in the tendon reflexes, and sometimes ankle-clonus shortly before the uremic outbreak, though a moderate increase was not uncommon in chronic nephritis in the absence of uremic symptoms. With improvement or recovery he found a return of the reflexes to normal.

During narcosis from ether and chloroform, Goldflam[8] found ankle-clonus frequently. Strümpell and Sternberg mention increased tendon reflexes in acute strychnine poisoning, but do not state whether clonus was present. Lewandowsky[9] states that Syllaba and Crocq noted clonus in chronic mercurial poisoning, but the writer was unable to find a reference to the original article. While chronic alcoholism increases the tendon reflexes it does not apparently give rise to clonus in the absence of organic changes.

An interesting state of the reflexes is found after the use of hyoscine (scopolamine) in medicinal doses. Ankle-clonus was noted in from one-quarter to one-half the cases by Hahn,[10] Kutner,[11] and Link,[12] and more remarkable still there was a positive Babinski toe sign in a still greater proportion, up to 86 per cent. The Babinski sign appeared in about one-half hour after administration, and after a minimum dose of 0.0004 gm. This production of a positive toe sign indicates a curious selective action on the part of hyoscine not to be found after the use of any other drug, and is one of the few exceptions to the rule that a positive Babinski, when found in adults, indicates organic nervous disease. The tendon reflexes after hyoscine showed no consistent changes, and the muscle tonus was said to be diminished.

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[5] Die Sehnenreflexe u. ihre Bedeutung f. d. Pathologie des Nervensystems, Leipzig, 1893, pp. 95 to 97.

[6] Verhandl. d. Kongress f. innere Med., 1909, xxvi, 341.

[7] Zeitschr. f. klin. Med., 1903, l, 257.

[8] Neurol. Centralblatt, 1903, xxii, 1109, 1137.

[9] Handb. d. Neurologie, 1910, i^2, 603.

Ankle-clonus in Neuroses and Pyschoses. In epilepsy, according to Gowers,[13] ankle-clonus is often to be found immediately after the convulsion, but only for a short time, and Babinski[14] has found his toe sign usually positive at this time.

The occurrence of ankle-clonus in neurasthenia is denied by many authorities, but Oppenheim[15] in his text-book states that it may be found, though rarely. Its presence should make one dissatisfied with the diagnosis of neurasthenia, for in most such cases some organic disease will be found. An instance in point is a case originally reported by Ballet[16] as one of neurasthenia, with ankle-clonus, but shown by the autopsy some years later to have been syphilitic meningitis.

In the case of hysteria there is also much difference of opinion. Most authorities are agreed that ankle-clonus does not occur in hysteria unless there is paralysis, and that it is absent in the common flaccid type of paralysis. In the hysteric spastic paraplegia, with contracture, however, ankle-clonus has been described by many authors, chiefly of the German school. Oppenheim and von Monakow[17] consider it rare, while Strümpell[18] says it is often encountered in this form of paralysis. Babinski[19] claims that when clonus is met with in hysteria it is always due to some extraneous factor, such as organic disease or excessive fatigue. The presence of ankle-clonus in hysteric subjects should therefore always arouse a suspicion of organic nervous disease, which becomes a certainty if the Babinski toe sign is present, for this is never met with in uncomplicated hysteria.

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[10] Neurol. Centralblatt, 1911, xxx, 114, 185.

[11] Deutsch. med. Woch., 1907, xxxiii, 98.

[12] Zeitschr. f. klin. Med., 1906, lix, 252.

[13] Epilepsy and Other Chronic Convulsive Diseases, London, 1901, 2d edit.

[14] Rev. neurologique, 1899, vii, 512.

[15] Lehrbuch d. Nervenkrankheiten, V Auflage, 1908.

[16] Rev. neurologique, 1903, xi, 234; 1905, xiii, 732.

[17] Gehirnpathologie, II Auflage, 1905, p. 489.

[18] Lehrbuch d. spec. Path. u. Therap., XIII Auflage, Band iii, S. 615.

[19] L'Encéphale, Paris, 1909, iv, 40.

In paralysis agitans, according to Oppenheim, the tremor of the foot may simulate clonus, and very rarely a true clonus may be present.

Bonhoeffer[20] and Westphal[21] have found transitory ankle-clonus, with spastic gait, in acute psychoses in the stage of excitement and loss of weight; Bonhoeffer speaks of his cases as psychosis with anxiety ("Angstpsychosen"), without giving a more definite diagnosis.

Ankle-clonus in Arthritis. It is important to remember that chronic disease of a joint often causes increased reflexes of the corresponding limb, and if the ankle is involved, ankle-clonus is by no means uncommon, apart from any organic nervous disease. In acute articular rheumatism clonus has not been reported, probably owing to the immobilization of the joints by muscle spasm. Jones[22] mentions the presence of jaw-clonus when the articulations of the jaw are involved. Clonus may occur in various types of chronic arthritis. Thus the writer has seen it in the gonococcal and chronic infectious types, while Jones emphasizes it in rheumatoid arthritis. The mechanism of its production is not clear, but might be explained on the ground that frequent painful stimuli from the joint put the corrresponding segment of the cord into a state of overexcitability, so that the stimulation of the Achilles tendon results in clonus.

Ankle-clonus after Fatigue. Several authors state that ankle-clonus may be found after unusual fatigue, or loss of sleep combined with anxiety, and Auerbach[23] found clonus in 2 out of 39 bicyclists after long distance (50 to 100 km.) races. After long-distance runs, however, the results are different, Knapp and Thomas[24] and Oeconomakis[25] finding no instances of clonus, but rather a diminution of the tendon reflexes, after "Marathon" races of 42 km. The difference may be due, as Oeconomakis suggests, to the fact that the calf muscles are comparatively little used in bicycling, while in running there is a chance for the reflex arc to become exhausted.

Graphic Studies of Ankle-clonus. The most extensive investigation of clonus by graphic methods has been made by Levi.[26] He found that the clonus associated with organic disease showed in the tracing oscillations of equal height and equally spaced, while in the pseudoclonus found in functional diseases and in convalescence from acute infections (only one case studied) the oscillations were of unequal height, giving an irregular appearance to the curve. In one of his cases, diagnosticated as hysteroneurasthenia, the clonus to the naked eye seemed to be genuine, and only the tracing proved it to be "false." Levi claims that true clonus is always a sign of organic disease, provided that the graphic method has been employed. The string galvanometer of Einthoven has also been used by Salomonson[27] in the study of clonus, and he, too, found a perfectly regular curve in the case of organic disease, while hysteria showed, besides the action currents of the clonus, those of voluntary muscle tetanus. These methods appear to offer a valuable way of studying clonus, but the observations have not been extended enough to be conclusive. It is desirable that further studies with them should be made in cases of ankle-clonus without organic disease of the nervous system.

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[20] Seitenstrangerscheinungen bei akuten Psychosen. Psychiatrische Abhandlungen herausgeg. v. C. Wernicke, Breslau, 1896, Heft ii, p. 1.

[21] Neurolog. Centralbl., 1903, xxii, 12 (foot-note).

[22] Lancet, 1902, ii, 1746.

[23] Neurolog. Centralbl., 1905, xxiv, 251.

[24] Jour. Nerv. and Ment. Dis., 1904, xxxi, 94.

[25] Neurol. Centralbl., 1907, xxvi, 498, 563.

[26] Arbeiten. a. d. Neurolog. Institut. a. d. Wiener Universität, 1907, xvi, 27.

The State of the Skin and Tendon Reflexes. In the class of cases under consideration the skin reflexes may be increased or diminished, but Babinski's toe sign is almost invariably absent, an important distinction from clonus due to organic disease, where it is usually to be elicited. The sole exceptions to this rule are clonus after the use of hyoscine and immediately after the epileptic convulsion, in both of which conditions a positive Babinski is the rule. The same holds true of Oppenheim's sign. The tendon reflexes are usually but not always increased, when clonus is present, whether it be due to organic or functional disease.

Pathological Anatomy of Clonus Unassociated With Organic Disease. Up to the present but three cases have been studied anatomically, viz., those of Strümpell,[28] Sternberg,[29] and the writer's first case. Strümpell's case was one dying of phthisis, and the spinal cord was found normal, both macroscopically and microscopically. This, however, was in 1873, before the introduction of the finer stains for nervous tissue. Sternberg's case was also one of phthisis, and the spinal cord is said to have been normal on microscopic examination, but no details are given. In the writer's case foci of myelitis were found in the posterior columns in the bulb, as well as diffuse Marchi degenerations. Not too much stress should be laid on the latter, however, for Gay and Southard[30] found such diffuse changes in a considerable proportion of cases dying of acute terminal infections. Further studies, including both brain and spinal cord, are necessary before the question of the absence of "organic" changes can be settled.

Explanation of the Occurrence of Clonus in the Absence of Organic Nervous Changes. It will be remarked that practically all the conditions under discussion are accompanied by toxemia, usually of a serious nature. Even in the case of clonus after excessive fatigue there is reason to believe that toxic products are at work. It is possible that the deleterious substances affect only the function of the nervous tissue, but it is also not improbable that there are structural changes, such as Edinger,[31] for instance, has shown to take place in rats after overexertion. Such changes, however, must be capable of complete recovery, for the clonus may disappear quickly, not to return. We are still in doubt as to the exact way in which clonus is produced. If, with Oppenheim, we regard ankle-clonus simply as an exaggeration of the Achilles reflex, we might suppose that the toxic substances rendered the nerve fibers, or perhaps the synapse in the cord, more irritable. The phenomenon cannot be accounted for solely by the removal of cortical inhibition by reason of a lesion of the pyramidal tracts, for clonus is sometimes found in cases of organic disease where these tracts are uninjured, and it may be lacking where they are completely degenerated. The bulbar lesions in the writer's first case are suggestive of the possibility that bulbospinal or bulbothalamal tracts might be of importance in the production of ankle-clonus.

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[27] Folia neuro-biol., 1910, iv, 1.

[28] Loc. cit.

[29] Loc. cit.

[30] Centralbl. f. Bakt., Parasitenkunde u Infectionskrank., 1910, lv, 117.

Diagnostic Considerations. The fact that ankle-clonus may appear in so many and varied conditions of toxemia, quite apart from any demonstrable lesion of the central nervous system, makes it necessary to restrict the diagnostic importance heretofore attached to this sign. In the absence of these toxic states, however, it has still a great deal of practical value in the diagnosis of organic nervous disease. The probability of such disease is greatly enhanced if there is in addition to clonus a positive Babinski or Oppenheim sign, as these do not occur in the toxic conditions under discussion, with the exception of hyoscine intoxication and the epileptic attack. The presence of a positive Mendel sign (plantar flexion of the toes on percussing the outer border of the foot over the fifth metatarsal bone), although considerably rarer than the other toe phenomena, appears to be conclusive evidence of organic disease. The complete absence of spasticity and of other signs pointing to organic lesions is also of importance in distinguishing the "functional," or "toxic" cases. On account of the rarity of true clonus in uncomplicated neurasthenia and hysteria its presence should always arouse the suspicion of coëxisting organic disease of the nervous system.

Prognostic Value. In the infectious diseases the appearance of ankle-clonus certainly adds to the gravity of the prognosis, as it indicates a high degree of toxemia, but it does not preclude the possibility of recovery. In nephritis it may be an important sign of the approaching uremic outbreak. The disappearance of the clonus is a favorable sign, except in the severest cases, where it may be only an indication of impending death.

1. SUMMARY AND CONCLUSIONS. Ankle-clonus indistinguishable from the genuine may be found more or less frequently in a variety of conditions, without accompanying organic nervous disease.

[31] Verhandl d. Kongress f. inn. Med., 1898, xvi, 292.

2. These conditions are: (*a*) Acute infectious diseases, especially typhoid; (*b*) chronic infections associated with marked toxemia, especially tuberculosis of the lungs in the third stage; (*c*) uremia shortly before and during the acute uremic seizure; (*d*) epilepsy immediately after the convulsion; (*e*) intoxication from certain drugs, *e. g.*, hyoscine, ether, and chloroform; (*f*) excessive fatigue; (*g*) exceptional cases of certain neuroses, viz., neurasthenia, hysteria, paralysis agitans; (*h*) psychoses in the stage of excitement; (*i*) chronic articular rheumatism.

3. With the exception of joint disease, a toxic action on the nervous system may be assumed in all these states as the underlying factor in the production of clonus. This is obvious in the case of the infectious diseases and drug intoxications; in uremia, epilepsy, and undue fatigue the presence of toxic products of metabolism may be regarded as probable, though not yet demonstrated, and even in hysteria and neurasthenia the action of toxic products in severe cases cannot be excluded.

4. In the case of articular rheumatism a constant spinal irritation from the inflamed joint tissues is the probable cause.

5. In two autopsies on cases of phthisis, with clonus, no changes were found in the central nervous system. In the writer's case, however, inflammatory exudate was demonstrated about the posterior median artery in the posterior septum of the bulb.

6. Clonus due to toxic states usually may be distinguished from that of organic nervous disease by the absence of spasticity and of other signs pointing to organic disease, and particularly by the absence of the Babinski and Oppenheim toe signs.

7. An exception to the above rule is encountered after the use of hyoscine in medicinal doses and immediately after the epileptic attack, in both of which instances the Babinski and Oppenheim signs may be positive.

8. The occurrence of ankle-clonus is of prognostic value in uremia, preceding at times the acute seizure. Ankle-clonus usually disappears a few days before death, otherwise its disappearance usually indicates an improvement in the patient's condition.

THE RATIONAL TREATMENT OF SURGICAL OR NON-PULMONARY TUBERCULOSIS.

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I do not intend this article to be an argument against the proper use of surgery in surgical tuberculosis. I shall endeavor to show,